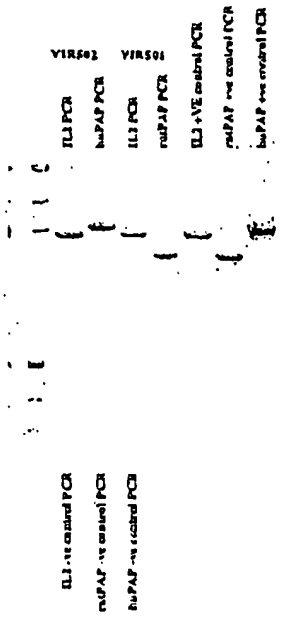


FIGURE 1

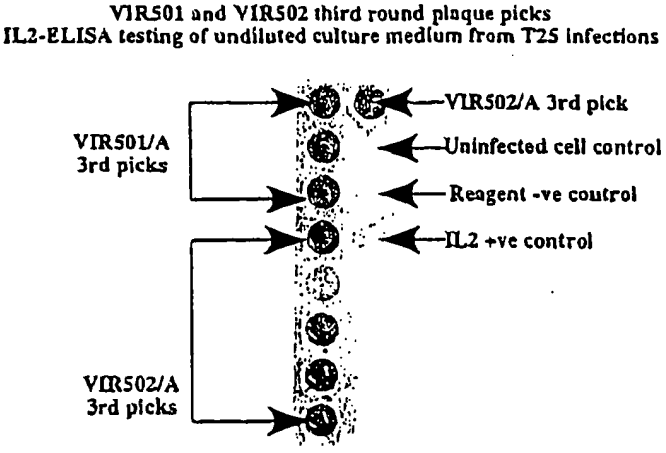

VIR501 and VIR502 third round plaque picks
IL2-ELISA testing of undiluted culture medium from T25 infections
VIR502/A 3rd pick
Uninfected cell control
Reagent -ve control
IL2 +ve control
VIR501/A
3rd picks
VIR502/A
3rd picks

FIGURE 2

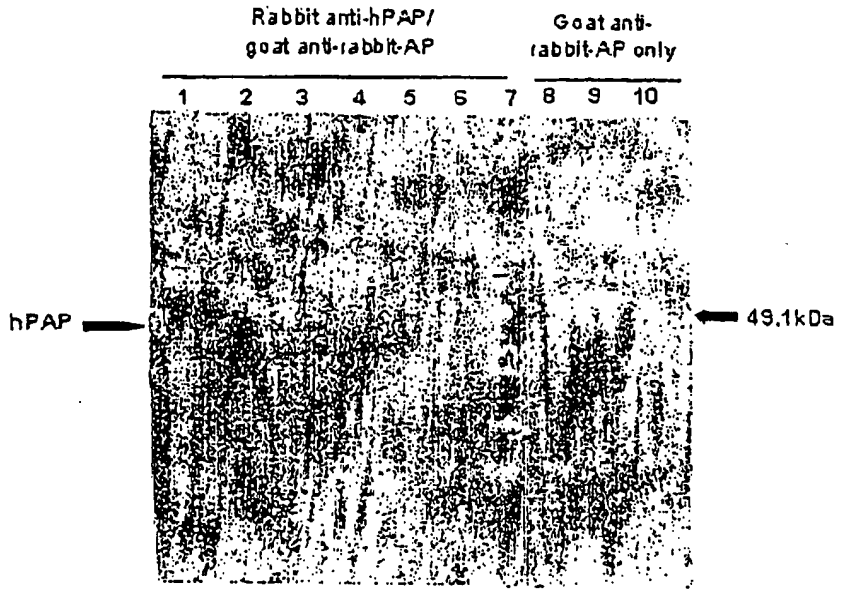

Rabbit anti-hPAP/
goat anti-rabbit-AP
Goat anti-
rabbit-AP only
1 2 3 4 5 6 7 8 9 10
hPAP
49.1kDa

FIGURE 3

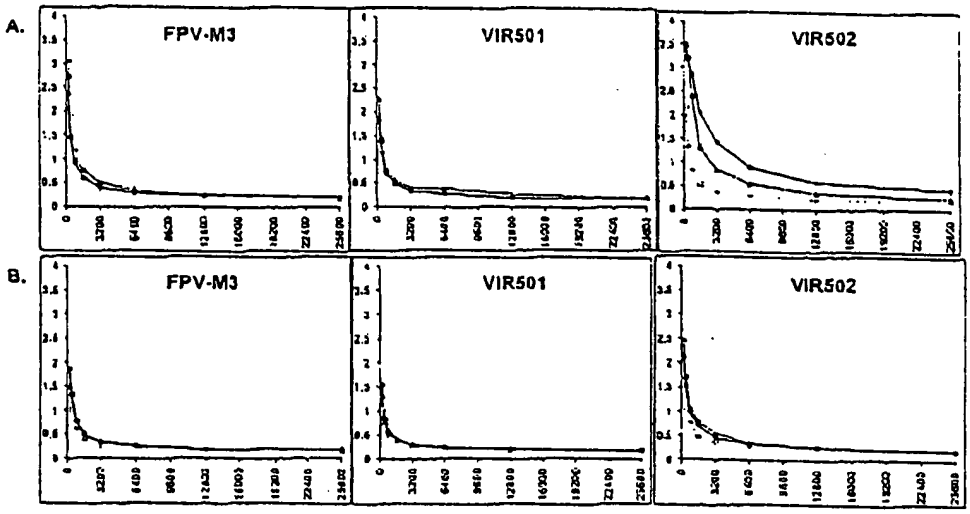


FIGURE 4

Insertion site of VIR501 containing human IL2 and rat PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

```
ATGGATAGAAATATCAATTTTAGTCCTGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAAGGTATTTT
TACCTATCTTTATAGTTAAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCATAAAA

TATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTTCTTTAAGGAAGAAATATTATATACATTTTTCCG
ATATATAATCAAAAACTTCATTATCATCGAAACTAATATAACTTAAAAAAGAAATTCCTTCTTTATAATATATGTAAAAAAGGC
FPV132R ORF in bold →

TTAGCTAAGCCTTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAAATGTGAAGAAGATGGATCTTTGATGATT
AATCGATTCGGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCTAGAAACTACTAA

TCGAGACCTTCCGGTATCTATTCGGCCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAGTTTGCTTTTATCGTCA
AGCTCTGGAAGGCCATAGATAAGCCGGAACTCAAATCTACCAAGTGGCCATTCCTAAAGGCTAACATCAAACGAAAATAGCAGT

ATAAATGGCGCATCCTCATCAACATCTCCTTACTCTATTTTTAACAGACGATAACGGATTTTATTCTTATCTATCCGAAAAAAG
TATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAATTGTCTGCTATTGCCTAAAATAAGAATAGATAGGCTTTTTC

TGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAGCGTTCTTATACGTTCTAAAGAGAA
ACTACTACTTCGAGAACTTCTGTATTTATGATAATTCTTTATATACCTGAAATAAGATTCGCAAGAATATGCAAGATTTCTCTT

ACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTTAAGGCTCTTATTAAAGTAAAGGATGATGGTACTTTAGT
TGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCCGAGAATAATTTCATTTCCTACTACCATGAAATCA

AAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCCGAAGAGATAGTTTTAGATAGAGGTTATACTTCGGATTTTGCTATAAG
TTTTCGTAAATGGTTCGGTAACAATTTAGGAGTAAGGCTTTTCTATCAAAATCTATCTCCAATATGAAGCCTAAAACGATATTC

CGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATACAAAATACATAAATCCAAACGAGAATATGTATATAAA
GCATTATTCTGATAGATCATTTTCGTCAATATATGAAGGGCGTTTATGTTTTATGTATTTAGGTTTGCTCTTATACATATATTT

CAACCTAATATCACTACTGAAGCGCAACTAGATCTTCCAAACCCACCCGCTTTTTATAGTAAGTTTTTCACCCATAAATAATAA
GTTGGATTATAGTGATGACTTCGCGTTGATCTAGAAGGTTTGGGTGGGCGAAAAATATCATTCAAAAAGTGGGTATTTATTATT
                                    vaccinia p7.5 promoter in bold & italic →

ATACAATAATTAATTTCTCGTAAAAGTAGAAAATATATTCTAATTTATTGCACGGTCTAGAACTAGTGgatccATGTACAGGAT
TATGTTATTAATTAAAGAGCATTTTCATCTTTTATATAAGATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCCTA
                                                                    > M  Y  R  M

GCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAA
CGTTGAGGACAGAACGTAACGTGATTAAGAACGTGAACAGTGTTTGTCACGTGGATGAAGTTCAAGCTGTTTCTTTTGTTTCTT
>  Q  L  L  S  C  I  A  L  I  L  A  L  V  T  N  S  A  P  T  S  S  S  T  K  K  T  K  K
   human IL2 protein coding sequence →

AACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACTCAC
TTGTGTCGATGTTGACCTCGTAAATGACGACCTAAATGTCTACTAAAACTTACCTTAATTATTAATGTTCTTAGGGTTTGAGTG
>  T  Q  L  Q  L  E  H  L  L  L  D  L  Q  M  I  L  N  G  I  N  N  Y  K  N  P  K  L  T

CAGGATGCTCACATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACC
GTCCTACGAGTGTAAATTCAAAATGTACGGGTTCTTCCGGTGTCTTGACTTTGTCGAAGTCACAGATCTTCTTCTTGAGTTTGG
>  R  M  L  T  F  K  F  Y  M  P  K  K  A  T  E  L  K  Q  L  Q  C  L  E  E  E  L  K  P

TCTGGAGGAAGTGCTGAATTTAGCTCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGT
AGACCTCCTTCACGACTTAAATCGAGTTTCGTTTTTGAAAGTGAATTCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCA
>  L  E  E  V  L  N  L  A  Q  S  K  N  F  H  L  R  P  R  D  L  I  S  N  I  N  V  I  V

TCTGGAACTAAAGGGATCTGAAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATG
AGACCTTGATTTCCCTAGACTTTGTTGTAAGTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGTCTAC
>  L  E  L  K  G  S  E  T  T  F  M  C  E  Y  A  D  E  T  A  T  I  V  E  F  L  N  R  W
```

FIGURE 5

```
GATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATTTTTTGTaGATCTGTCGACCATTTAGTATCCTAAAATTGAA
CTAATGGAAAACAGTTTCGTAGTAGAGTTGTGATTGAACTAAAAACAtcTAGACAGCTGGTAAATCATAGGATTTTAACTT
> I T F C Q S I I S T L T .                                    FPV early/late
promoter
                                        Early transcriptional
                                        stop sequence (bold)

TTGTAATTATCGATAATAAATGAGAGCTGTCCCTCTGCACCTCGTCGGGACAGCAAGCCTCACCCTTGGCTTCTTGCTCCTGCT
AACATTAATAGCTATTATTTACTCTCGACAGGGAGACGTGGAGCAGCCCTGTCGTTCGGAGTGGGAACCGAAGAACGAGGACGA
                    > M R A V P L H L V G T A S L T L G F L L L L
                      Rat PAP protein coding sequence

ATCTCTCCGCCTGGACCCAGGCCAAGCCAAGGAGTTGAAGTTTGTGACATTGGTGTTCCGGCATGGAGACCGAGGTCCCATCGA
TAGAGAGGCGGACCTGGGTCCGGTTCGGTTCCTCAACTTCAAACACTGTAACCACAAGGCCGTACCTCTGGCTCCAGGGTAGCT
> S L R L D P G Q A K E L K F V T L V F R H G D R G P I E

GACCTTTCCTAATGACCCCATTAAGGAATCCTCGTGGCCACAAGGATTTGGCCAACTCACCAAGTGGGGCATGGGACAGCACTA
CTGGAAAGGATTACTGGGGTAATTCCTTAGGAGCACCGGTGTTCCTAAACCGGTTGAGTGGTTCACCCCGTACCCTGTCGTGAT
> T F P N D P I K E S S W P Q G F G Q L T K W G M G Q H Y

CGAACTCGGAAGTTATATAAGGAGAAGATACGGGAGATTCTTGAACAACTCCTATAAACATGACCAGGTTTATATCCGAAGCAC
GCTTGAGCCTTCAATATATTCCTCTTCTATGCCCTCTAAGAACTTGTTGAGGATATTTGTACTGGTCCAAATATAGGCTTCGTG
> E L G S Y I R R R Y G R F L N N S Y K H D Q V Y I R S T

AGATGTTGACAGGACTCTGATGAGCGCTATGACAAACCTCGCAGCCCTGTTTCCCCCTGAGGGGATCAGCATCTGGAATCCCAG
TCTACAACTGTCCTGAGACTACTCGCGATACTGTTTGGAGCGTCGGGACAAAGGGGGACTCCCCTAGTCGTAGACCTTAGGGTC
> D V D R T L M S A M T N L A A L F P P E G I S I W N P R

ACTGCTCTGGCAGCCCATCCCAGTGCACACCGTGTCTCTCTCTGAGGATCGGTTGCTATACCTGCCTTTCAGGGACTGTCCTCG
TGACGAGACCGTCGGGTAGGGTCACGTGTGGCACAGAGAGAGACTCCTAGCCAACGATATGGACGGAAAGTCCCTGACAGGAGC
> L L W Q P I P V H T V S L S E D R L L Y L P F R D C P R

CTTTCAAGAACTCAAGAGTGAGACTTTAAAATCTGAGGAGTTCCTGAAGAGGCTTCAACCATATAAAAGCTTCATAGACACCTT
GAAAGTTCTTGAGTTCTCACTCTGAAATTTTAGACTCCTCAAGGACTTCTCCGAAGTTGGTATATTTTCGAAGTATCTGTGGAA
> F Q E L K S E T L K S E E F L K R L Q P Y K S F I D T L

GCCATCGCTGTCGGGATTCGAGGACCAGGATCTTTTTGAAATCTGGAGTAGGCTTTACGACCCTTTATATTGCGAGAGTGTTCA
CGGTAGCGACAGCCCTAAGCTCCTGGTCCTAGAAAAACTTTAGACCTCATCCGAAATGCTGGGAAATATAACGCTCTCACAAGT
> P S L S G F E D Q D L F E I W S R L Y D P L Y C E S V H

CAATTTCACCTTCCGCACCTGGGCCACAGAGGACGCCATGACTAAGTTGAAGGAGTTGTCAGAATTATCTCTGTTATCTCTTTA
GTTAAAGTGGAAGGCGTGGACCCGGTGTCTCCTGCGGTACTGATTCAACTTCCTCAACAGTCTTAATAGAGACAATAGAGAAAT
> N F T F R T W A T E D A M T K L K E L S E L S L L S L Y

TGGAATTCACAAGCAGAAAGAGAAATCTAGACTCCAGGGGGGCGTCCTGGTCAATGAAATTCTCAAGAACATGAAGCTTGCAAC
ACCTTAAGTGTTCGTCTTTCTCTTTAGATCTGAGGTCCCCCCGCAGGACCAGTTACTTTAAGAGTTCTTGTACTTCGAACGTTG
> G I H K Q K E K S R L Q G G V L V N E I L K N M K L A T

TCAACCACAGAAGGCCAGGAAGTTGATCATGTATTCTGCATATGACACTACTGTGAGTGGCCTGCAGATGGCGCTAGAGCTTTA
AGTTGGTGTCTTCCGGTCCTTCAACTAGTACATAAGACGTATACTGTGATGACACTCACCGGACGTCTACCGCGATCTCGAAAT
> Q P Q K A R K L I M Y S A Y D T T V S G L Q M A L E L Y

TAATGGACTTCTACCTCCCTACGCTTCCTGCCACATAATGGAATTGTACCAGGATAATGGGGGGACCTTCGTGGAGATGTACTA
ATTACCTGAAGATGGAGGGATGCGAAGGACGGTGTATTACCTTAACATGGTCCTATTACCCCCCTGGAAGCACCTCTACATGAT
> N G L L P P Y A S C H I M E L Y Q D N G G T F V E M Y Y

CCGGAATGAGACCCAGAACGAGCCCTACCCACTCACGCTGCCGGGCTGTACCCACAGCTGCCCTCTGGAGAAGTTTGCAGAGCT
GGCCTTACTCTGGGTCTTGCTCGGGATGGGTGAGTGCGACGGCCCGACATGGGTGTCGACGGGAGACCTCTTCAAACGTCTCGA
> R N E T Q N E P Y P L T L P G C T H S C P L E K F A E L
```

FIGURE 5 cont.

ACTGGACCCCGTGATCCCCCAGGACTGGGCCACAGAGTGTATGGGCACAAGCAACCACCAAGCGTCGCTGTAATTTTTCTGTCG
TGACCTGGGGCACTAGGGGGTCCTGACCCGGTGTCTCACATACCCGTGTTCGTTGGTGGTTCGCAGCGACATTAAAAAGACAGC
> L D P V I P Q D W A T E C M G T S N H Q A S L .

ACCCATGGTTGTTAAAAAGGAATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTT
TGGGTACCAACAATTTTTCCTTAACTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCCTGTAGTCCTCAGAAA
FPV134R ORF in bold

TAAAGAACTTGAAATGACAAAACCTTATATGTTCTTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTC
ATTTCTTGAACTTTACTGTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTTCTGATATTGTTTCTCAATCTTTTAAG

TAATACTAAGTTTCAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAACTTTATTTCTTAAATACATTAATCAAGAATAAAAC
ATTATGATTCAAAGTTCCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAAATAAAGAATTTATGTAATTAGTTCTTATTTTG

GTTATGTTCAGATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAATTTTTTTATATCATTATATGGATGA
CAATACAAGTCTATGTCAATAGCACATATATCCCAGTCGTGGTCCTTCGGTATATTTAAAAAATATAGTAATATACCTACT
Early transcriptional
stop sequence for rat PAF

TCTTAAAATAGATTTAAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAAAATGTGTCTATAAT
AGAATTTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTTACACAGATATTA

ACATAGGTTTGTAGATGAACAATACTTGTTTAAGCTACGTAATATGATTAGGAAAAACCATAAAATTGTACTGATATCAGATAT
TGTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTTGGTATTTTAACATGACTATAGTCTATA

TAGATCGCTAAGAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCATTCTTAA
ATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGTCTTAGTTTACCATTCGTAAGAATT

ACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTTCCGGATCAGTGGATAAGAGACTTTTACATTCCTTGTGGAGATGAGTT
TGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACACCTCTACTCAA

T
A

FIGURE 5 cont.

Insertion site of VIR502 containing human IL2 and human PAP sequences

The FPV ORFs are with reference to FPV genome ORFs – Genbank Ac No.: AF198100

```
ATGGATAGAAATATCAATTTTAGTCCTGTATTTATAGAACCTAGGTTTAAACACGAGTTTCTATTATCTCCTCAAACGTA
TACCTATCTTTATAGTTAAAATCAGGACATAAATATCTTGGATCCAAATTTGTGCTCAAAGATAATAGAGGAGTTTCCAT
FPV132R ORF in bold →

TTTTTATATATTAGTTTTTGAAGTAATAGTAGCTTTGATTATATTGAATTTTTTCTTTAAGGAAGAAATATTATATACAT
AAAAATATATAATCAAAAACTTCATTATCATCGAAACTAATATAACTTAAAAAAGAAATTCCTTCTTTATAATATATGTA

TTTTTCCGTTAGCTAACCCTTCTAAAAATTCAATAAATAGTCTGCTGGATAGAACTATGTTAAAATGTGAAGAAGATGGA
AAAAAGGCAATCGATTCGGAAGATTTTTAAGTTATTTATCAGACGACCTATCTTGATACAATTTTACACTTCTTCTACCT

TCTTTGATGATTTCCAGACCTTCCGGTATCTATTCGGCCTTGAGTTTAGATGGTTCACCGGTAAGGATTTCCGATTGTAG
AGAAACTACTAAAGCTCTGGAAGGCCATAGATAAGCCGCAACTCAAATCTACCAAGTGGCCATTCCTAAAGGCTAACATC

TTTGCTTTTATCGTCAATAAATGGCGCATCCTCATCAACATCTCCTTACTCTATTTTTAACAGACGATAACGGATTTTAT
AAACGAAAATAGCAGTTATTTACCGCGTAGGAGTAGTTGTAGAGGAATGAGATAAAAATTGTCTGCTATTGCCTAAAATA

TCTTATCTATCCGAAAAAAGTGATGATGAAGCTCTTGAAGACATAAATACTATTAAGAAATATATGGACTTTATTCTAAG
AGAATAGATAGGCTTTTTTCACTACTACTTCGAGAACTTCTGTATTTATGATAATTCTTTATATACCTGAAATAAGATTC

CGTTCTTATACGTTCTAAAGAGAAACTAGAAAATATAGGATGTTCTTACGAGCCTATGAGTGAATCGTTTAAGGCTCTTA
GCAAGAATATGCAAGATTTCTCTTTGATCTTTTATATCCTACAAGAATGCTCGGATACTCACTTAGCAAATTCCGAGAAT

TTAAAGTAAAGGATGATGGTACTTTAGTAAAAGCATTTACCAAGCCATTGTTAAATCCTCATTCCGAAAAGATAGTTTTA
AATTTCATTTCCTACTACCATGAAATCATTTTCGTAAATGGTTCGGTAACAATTTAGGAGTAAGGCTTTTCTATCAAAAT

GATAGAGGTTATACTTCGGATTTTGCTATAAGCGTAATAAGACTATCTAGTAAAAGCAGTTATATACTTCCCGCAAATAC
CTATCTCCAATATGAAGCCTAAAACGATATTCGCATTATTCTGATAGATCATTTTCGTCAATATATGAAGGGCGTTTATG

AAAATACATAAATCCAAACGAGAATATGTATATAAACAACCTAATATCACTACTGAAGCGCAACTAGATCTTCCAAACCC
TTTTATGTATTTAGGTTTGCTCTTATACATATATTTGTTGGATTATAGTGATGACTTCGCGTTGATCTAGAAGGTTTGGG

ACCCGCTTTTTATAGTAAGTTTTTCACCCATAAATAATAAATACAATAATTAATTTCTCGTAAAAGTAGAAAATATATTC
TGGGCGAAAAATATCATTCAAAAAGTGGGTATTTATTATTTATGTTATTAATTAAAGAGCATTTTCATCTTTTATATAAG
vaccinia p7.5 promoter in bold & italic →

TAATTTATTGCACGGTCTAGAACTAGTGGatccATGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACT
ATTAAATAACGTGCCAGATCTTGATCACctaggTACATGTCCTACGTTGAGGACAGAACGTAACGTGATTAAGAACGTGA
                                  > N  Y  R  M  Q  L  L  S  C  I  A  L  I  L  A  L
                                     Human IL2 protein coding sequence →

TGTCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAAACACAGCTACAACTGGAGCATTTACTGCTGG
ACAGTGTTTGTCACGTGGATGAAGTTCAAGCTGTTTCTTTTGTTTCTTTTGTGTCGATGTTGACCTCGTAAATGACGACC
>  V  T  N  S  A  P  T  S  S  S  T  K  K  T  K  K  T  Q  L  Q  L  E  H  L  L  L

ATTTACAGATGATTTTGAATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCACATTTAAGTTTTACATG
TAAATGTCTACTAAAACTTACCTTAATTATTAATGTTCTTAGGGTTTGAGTGGTCCTACGAGTGTAAATTCAAAATGTAC
>D  L  Q  M  I  L  N  G  I  N  N  Y  K  N  P  K  L  T  R  M  L  T  F  K  F  Y  M

CCCAAGAAGGCCACAGAACTGAAACAGCTTCAGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTAGC
GGGTTCTTCCGGTGTCTTGACTTTGTCGAAGTCACAGATCTTCTTCTTGAGTTTGGAGACCTCCTTCACGACTTAAATCG
>P  K  K  A  T  E  L  K  Q  L  Q  C  L  E  E  E  L  K  P  L  E  E  V  L  N  L  A

TCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAATATCAACGTAATAGTTCTGGAACTAAAGGGATCTG
AGTTTCGTTTTTGAAAGTGAATTCTGGGTCCCTGAATTAGTCGTTATAGTTGCATTATCAAGACCTTGATTTCCCTAGAC
>  Q  S  K  N  F  H  L  R  P  R  D  L  I  S  N  I  N  V  I  V  L  E  L  K  G  S
```

FIGURE 6

Michael Paul Brown, et al.
POXVIRUS VECTOR ENCODING
PROSTATE SPECIFIC ANTIGENS FOR
TREATMENT OF PROSTATE CANCER
Docket: 19610


```
AAACAACATTCATGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAACAGATGGATTACCTTTTGTCAA
TTTGTTGTAACTACACACTTATACGTCTACTCTGTCGTTGGTAACATCTTAAAGACTTGTCTACCTAATGGAAAACAGTT
>E  T  T  F  M  C  E  Y  A  D  E  T  A  T  I  V  E  F  L  N  R  W  I  T  F  C  Q

AGCATCATCTCAACACTAACTTGATTTTTGTaGATCTGtcgaccatttagtatcctaaaattgaattgtaattatcg
TCGTAGTAGAGTTGTGATTGAACTAAAAACAtCTAGACagctggtaaatcataggattttaacttaacattaatagc
> S  I  I  S  T  L  T  •                         FPV early late promoter →
                   Early transcriptional        in bold & italic
                   stop sequence in bold

ataataaATGAGAGCTGCACCCCTCCTCCTGGCCAGGGCAGCAAGCCTTAGCCTTGGCTTCTTGTTTCTGCTTTTTTCT
tattattTACTCTCGACGTGGGGAGGAGGACCGGTCCCGTCGTTCGGAATCGGAACCGAAGAACAAAGACGAAAAAAGA
      > M  R  A  A  P  L  L  L  A  R  A  A  S  L  S  L  G  F  L  F  L  L  F  F
        Human PAP protein coding sequence →

GGCTAGACCGAAGTGTACTAGCCAAGGAGTTGAAGTTTGTGACTTTGGTGTTTCGGCATGGAGACCGAAGTCCCATTGAC
CCGATCTGGCTTCACATGATCGGTTCCTCAACTTCAAACACTGAAACCACAAAGCCGTACCTCTGGCTTCAGGGTAACTG
>W  L  D  R  S  V  L  A  K  E  L  K  F  V  T  L  V  F  R  H  G  D  R  S  P  I  D

ACCTTTCCCACTGACCCCATAAAGGAATCCTCATGGCCACAAGGATTTGGCCAACTCACCCAGCTGGGCATGGAGCAGCA
TGGAAAGGGTGACTGGGGTATTTCCTTAGGAGTACCGGTGTTCCTAAACCGGTTGAGTGGGTCGACCCGTACCTCGTCGT
> T  F  P  T  D  P  I  K  E  S  S  W  P  Q  G  F  G  Q  L  T  Q  L  G  M  E  Q  H

TTATGAACTTGGAGAGTATATAAGAAAGAGATATAGAAAATTCTTGAATGAGTCCTATAAACATGAACAGGTTTATATTC
AATACTTGAACCTCTCATATATTCTTTCTCTATATCTTTTAAGAACTTACTCAGGATATTTGTACTTGTCCAAATATAAG
>  Y  E  L  G  E  Y  I  R  K  R  Y  R  K  F  L  N  E  S  Y  K  H  E  Q  V  Y  I

GAAGCACAGACGTTGACCGGACTTTGATGAGTGCTATGACAAACCTGGCAGCCCTGTTTCCCCCAGAAGGTGTCAGCATC
CTTCGTGTCTGCAACTGGCCTGAAACTACTCACGATACTGTTTGGACCGTCGGGACAAAGGGGGTCTTCCACAGTCGTAG
>R  S  T  D  V  D  R  T  L  M  S  A  M  T  N  L  A  A  L  F  P  P  E  G  V  S  I

TGGAATCCTATCCTACTCTGGCAGCCCATCCCGGTGCACACAGTTCCTCTTTCTGAAGATCAGTTGCTATACCTGCCTTT
ACCTTAGGATAGGATGAGACCGTCGGGTAGGGCCACGTGTGTCAAGGAGAAAGACTTCTAGTCAACGATATGGACGGAAA
> W  N  P  I  L  L  W  Q  P  I  P  V  H  T  V  P  L  S  E  D  Q  L  L  Y  L  P  F

CAGGAACTGCCCTCGTTTTCAAGAACTTGAGAGTGAGACTTTGAAATCAGAGGAATTCCAGAAGAGGCTGCACCCTTATA
GTCCTTGACGGGAGCAAAAGTTCTTGAACTCTCACTCTGAAACTTTAGTCTCCTTAAGGTCTTCTCCGACGTGGGAATAT
>  R  N  C  P  R  F  Q  E  L  E  S  E  T  L  K  S  E  E  F  Q  K  R  L  H  P  Y

AGGATTTTATAGCTACCTTGGGAAAACTTTCAGGATTACATGGCCAGGACCTTTTTGGAATTTGGAGTAAAGTCTACGAC
TCCTAAAATATCGATGGAACCCTTTTGAAAGTCCTAATGTACCGGTCCTGGAAAAACCTTAAACCTCATTTCAGATGCTG
>K  D  F  I  A  T  L  G  K  L  S  G  L  H  G  Q  D  L  F  G  I  W  S  K  V  Y  D

CCTTTATATTGTGAGAGTGTTCACAATTTCACTTTACCCTCCTGGGCCACTGAGGACACCATGACTAAGTTGAGAGAATT
GGAAATATAACACTCTCACAAGTGTTAAAGTGAAATGGGAGGACCCGGTGACTCCTGTGGTACTGATTCAACTCTCTTAA
> P  L  Y  C  E  S  V  H  N  F  T  L  P  S  W  A  T  E  D  T  M  T  K  L  R  E  L

GTCAGAATTGTCCCTCCTGTCCCTCTATGGAATTCACAAGCAGAAAGAGAAATCTAGGCTCCAAGGGGGTGTCCTGGTCA
CAGTCTTAACAGGGAGGACAGGGAGATACCTTAAGTGTTCGTCTTTCTCTTTAGATCCGAGGTTCCCCCACAGGACCAGT
>  S  E  L  S  L  L  S  L  Y  G  I  H  K  Q  K  E  K  S  R  L  Q  G  G  V  L  V

ATGAAATCCTCAATCACATGAAGAGAGCAACTCAGATACCAAGCTACAAAAAACTTATCATGTATTCTGCGCATGACACT
TACTTTAGGAGTTAGTGTACTTCTCTCGTTGAGTCTATGGTTCGATGTTTTTTGAATAGTACATAAGACGCGTACTGTGA
>N  E  I  L  N  H  M  K  R  A  T  Q  I  P  S  Y  K  K  L  I  M  Y  S  A  H  D  T

ACTGTGAGTGGCCTACAGATGGCGCTAGATGTTTACAACGGACTCCTTCCTCCCTATGCTTCTTGCCACTTGACGGAATT
TGACACTCACCGGATGTCTACCGCGATCTACAAATGTTGCCTGAGGAAGGAGGGATACGAAGAACGGTGAACTGCCTTAA
> T  V  S  G  L  Q  M  A  L  D  V  Y  N  G  L  L  P  P  Y  A  S  C  H  L  T  E  L
```

FIGURE 6 cont.

```
GTACTTTGAGAAGGGGGAGTACTTTGTGGAGATGTACTATCGGAATGAGACGCAGCACGAGCCGTATCCCCTCATGCTAC
CATGAAACTCTTCCCCCTCATGAAACACCTCTACATGATAGCCTTACTCTGCGTCGTGCTCGGCATAGGGGAGTACGATG
>  Y  F  E  K  G  E  Y  F  V  E  M  Y  Y  R  N  E  T  Q  H  E  P  Y  P  L  M  L

CTGGCTGCAGCCCTAGCTGTCCTCTGGAGAGGTTTGCTGAGCTGGTTGGCCCCTGTGATCCCTCAAGACTGGTCCACGGAG
GACCGACGTCGGGATCGACAGGAGACCTCTCCAAACGACTCGACCAACCGGGACACTAGGGAGTTCTGACCAGGTGCCTC
>P  G  C  S  P  S  C  P  L  E  R  F  A  E  L  V  G  P  V  I  P  Q  D  W  S  T  E

TGTATGACCACAAACAGCCATCAAGGTACTGAGGACAGTACAGATTAATTTTTCTGTCGACCCATGGTTGTTAAAAAGGA
ACATACTGGTGTTTGTCGGTAGTTCCATGACTCCTGTCATGTCTAATTAAAAAGACAGCTGGGTACCAACAATTTTTCCT
>C  M  T  T  N  S  H  Q  G  T  E  D  S  T  D  *

ATTGAAAGAAAATATTTTATATCGTAATAAATTAAATATGCATGAAGGACATCAGGAGTCTTTTAAAGAACTTGAAATGA
TAACTTTCTTTTATAAAATATAGCATTATTTAATTTATACGTACTTCCTGTAGTCCTCAGAAAATTTCTTGAACTTTACT
                                        FPV134 ORF in bold →

CAAAACCTTATATGTTCTTCAATGAACTAGTAGGTGAAGAAGACTATAACAAAGAGTTAGAAAATTCTAATACTAAGTTT
GTTTTGGAATATACAAGAAGTTACTTGATCATCCACTTCTTCTGATATTGTTTCTCAATCTTTTAAGATTATGATTCAAA

CAAGGACAGGGCCAGCTTAAGCTGTTATTAGGAGAACTTTATTTCTTAAATACATTAATCAAGAATAAAACGTTATGTTC
GTTCCTGTCCCGGTCGAATTCGACAATAATCCTCTTGAAATAAAGAATTTATGTAATTAGTTCTTATTTTGCAATACAAG

AGATACAGTTATCGTGTATATAGGGTCAGCACCAGGAAGCCATATAAATTTTTTTATATCATTATATGGATGATCTTA
TCTATGTCAATAGCACATATATCCCAGTCGTGGTCCTTCGCTATATTTAAAAAATATAGTAATATACCTACTAGAAT
                                                    Early transcriptional
                                                    stop sequence in bold
                                                    for human PAP sequence

AAATAGATTTAAAATGGATATTAATAGATGGTAGAGATCATGATCGATCTCTAGAAAGTCTTAAAAATGTGTCTATAATA
TTTATCTAAATTTTACCTATAATTATCTACCATCTCTAGTACTAGCTAGAGATCTTTCAGAATTTTTACACAGATATTAT

CATAGGTTTGTAGATGAACAATACTTGTTTAAGCTACGTAATATGATTAGGAAAAACCATAAAATTGTACTGATATCAGA
GTATCCAAACATCTACTTGTTATGAACAAATTCGATGCATTATACTAATCCTTTTTGGTATTTTAACATGACTATAGTCT

TATTAGATCGCTAAGAGGAAAAGAACCTACTAGCGAGGACCTATTACACGATTACGCGTTGCAGAATCAAATGGTAAGCA
ATAATCTAGCGATTCTCCTTTTCTTGGATGATCGCTCCTGGATAATGTGCTAATGCGCAACGTCTTAGTTTACCATTCGT

TTCTTAAACCAATAGCATCGAGCCTGAAATGGAGATGTCCGTTTCCGGATCAGTGGATAAGAGACTTTTACATTCCTTGT
AAGAATTTGGTTATCGTAGCTCGGACTTTACCTCTACAGGCAAAGGCCTAGTCACCTATTCTCTGAAAATGTAAGGAACA

GGAGATGAGTTT
CCTCTACTCAAA
```

FIGURE 6 cont.

Amino acid sequence alignment of rat PAP from VIR501 with human PAP from VIR502

Boxed: Identical amino acid

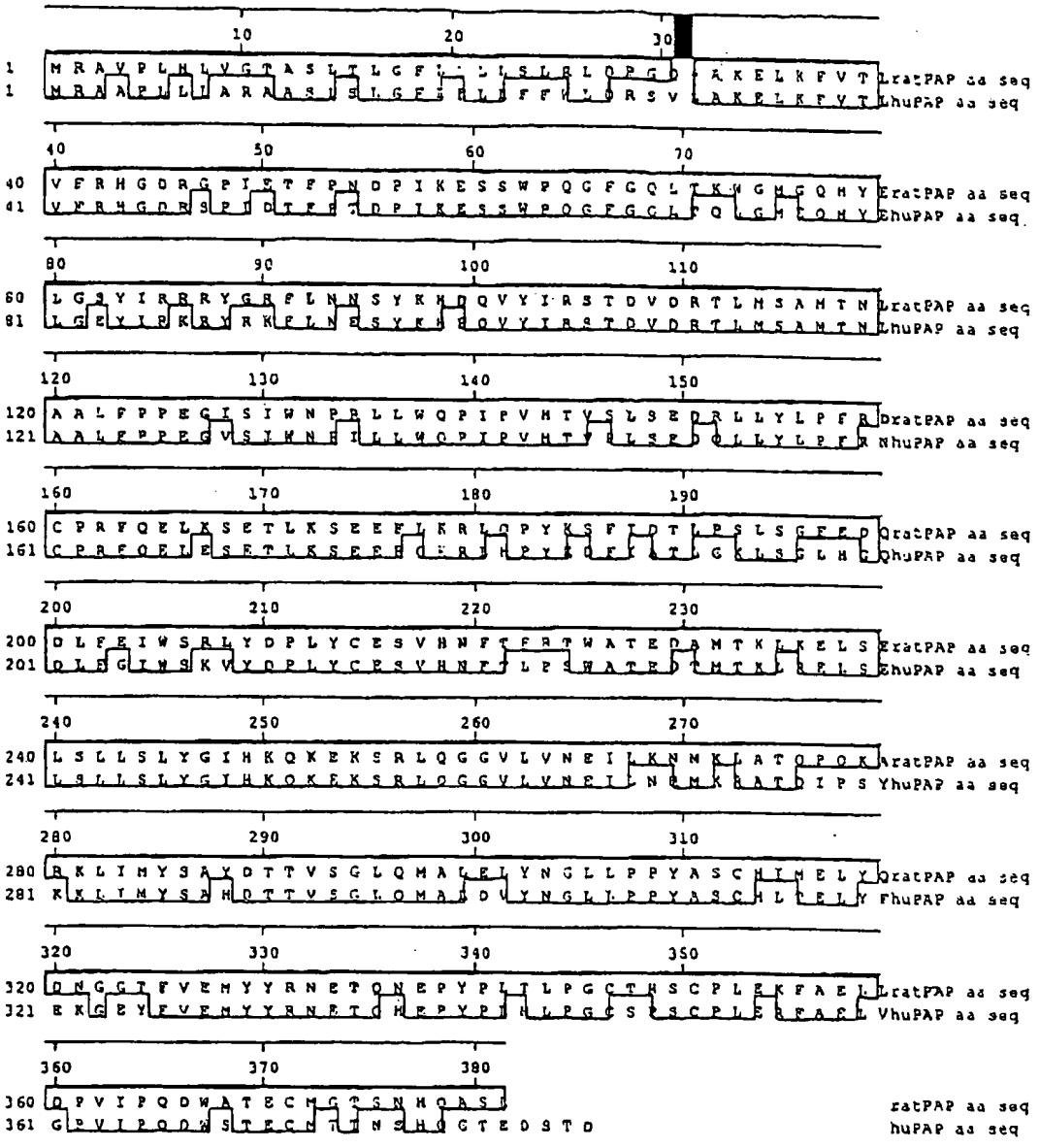


FIGURE 7

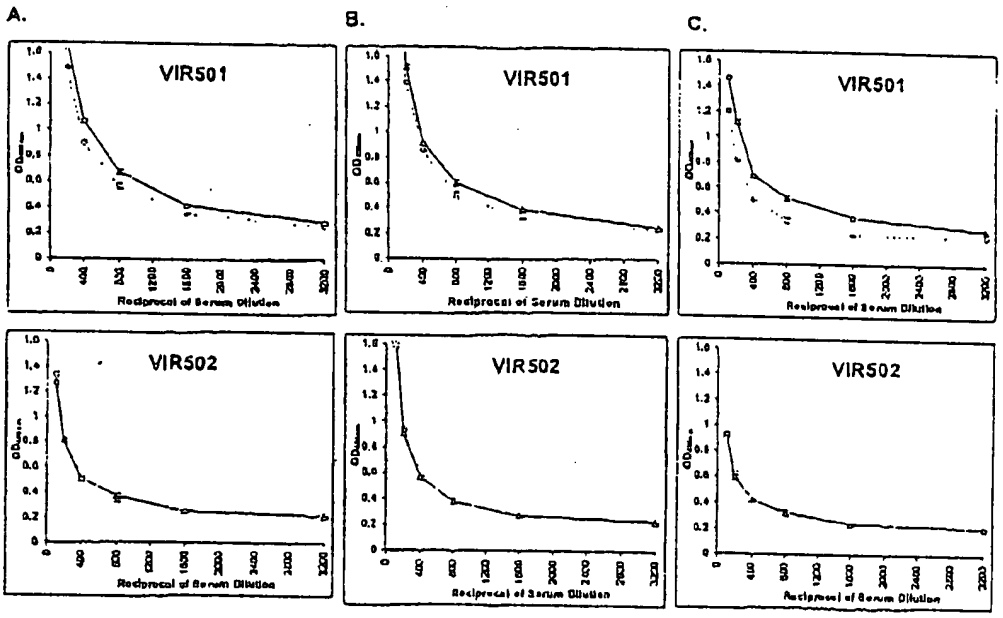

A.
B.
C.
VIR501
VIR501
VIR501
VIR502
VIR502
VIR502
Reciprocal of Serum Dilution

FIGURE 8

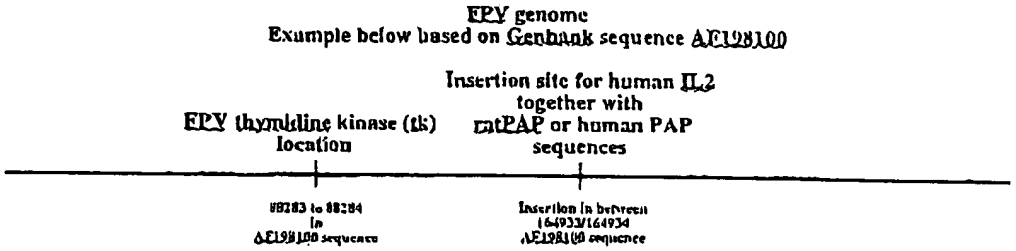
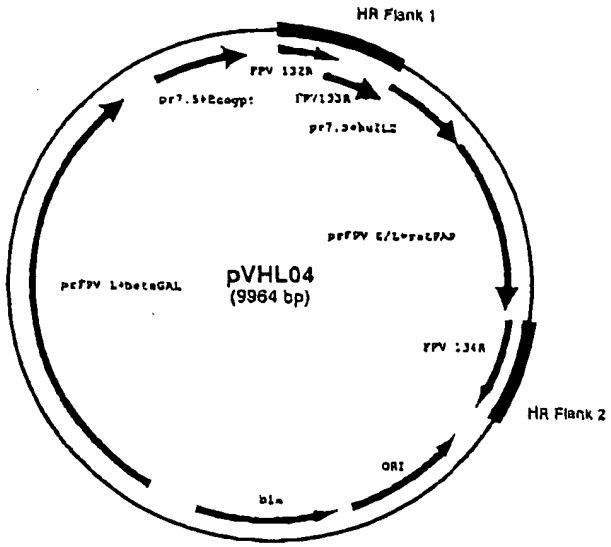

EPV genome
Example below based on Genbank sequence AF198100
Insertion site for human IL2
together with
rat PAP or human PAP
sequences
EPV thymidine kinase (tk)
location
88283 to 88284
in
AF198100 sequence
Insertion in between
164933/164934
AF198100 sequence

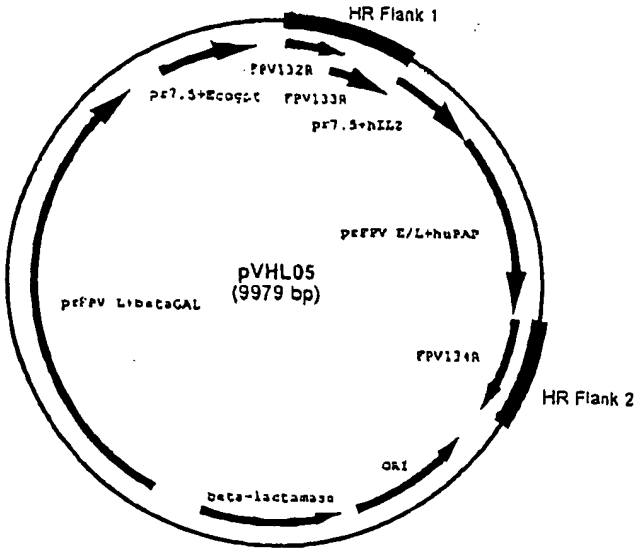
FIGURE 9



pVHL04 was constructed by cloning the following into a bacterial plasmid vector:

1. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
2. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
3. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs over lap each other. This sequence forms the homologous recombination flank 1.
4. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
5. prFPV E/L+rat PAP: rat prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
6. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

FIGURE 10



pVHL05 was constructed by cloning the following into a bacterial plasmid vector:

7. prFPV L+betaGAL: beta-Galactosidase protein coding sequence operatively linked to a fowlpox virus late promoter
8. pr7.5+Ecogpt: E coli xanthine-guanine phosphoribosyl transferase protein coding sequence operatively linked to a vaccinia virus p7.5 promoter
9. Fowlpox Virus nucleotide sequence spanning ORFs 132 and 133 – these two ORFs over lap each other. This sequence forms the homologous recombination flank 1.
10. pr7.5+huIL2: human IL2 protein coding sequence operatively linked to a vaccinia virus p7.5 promoter.
11. prFPV E/L+huPAP: human prostatic acid phosphatase (PAP) protein coding sequence operatively linked to a fowlpox virus early late promoter.
12. Fowlpox Virus nucleotide sequence spanning ORFs 134 - this sequence forms the homologous recombination flank 2.

FIGURE 11

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☑ FADED TEXT OR DRAWING
- ☑ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☑ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.